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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,830	05/10/2001	Arthur A. Vandenbark	P-IM 4734	6459

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EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/853,830	VANDENBARK, ARTHUR A.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *26-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Applicant's election with traverse of group I in Paper No. 12 is acknowledged. The traversal is on the ground(s) that it would not be undue burden to search the subject matter of groups II and III together with that of group I. Applicants arguments concerning groups I and II are persuasive. Accordingly, groups I and II have been examined herein. However, Applicants arguments concerning group III are not persuasive. Restriction of distinct inventions is proper if it can be shown that the inventions have a different classification, or have acquired a separate status in the art or have a different field of search (see MPEP 808.02). The claims of groups I and III have acquired a separate status in the art as recognized by their different classification and as recognized by their divergent subject matter, such that the claims group I are drawn to methods of identifying T cell receptor variable genes, whereas the claims of group III are drawn to kits comprising TCR V peptides and nucleic acid primers. A search of the distinct inventions would not be co-extensive as evidenced by the requirement for searching different keywords. For example a search for primers for the TCRV gene and for TCR V peptides would not lead one to all references teaching methods for identifying T cell receptor variable genes wherein the methods detect a TCR V gene and measure regulatory activity elicited in response to a TCR V peptide. Therefore, undue burden would be required to examine each of the claimed inventions. Accordingly, the requirement is still deemed proper and is therefore made FINAL.

2. The information disclosure statement filed in this application fails to include a concise statement of the relevance of the following non-English language reference listed, as required under 37 CFR § 1.98(a)(3): EP 957359. The above item of information has not been considered by the

examiner. The other items of information that are otherwise in compliance with the provisions of 37 CFR §1.97-1.98 have been considered by the examiner.

3. Claims 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23-25 are indefinite because it is unclear as to the relationship between steps (a) and (b). The claims are drawn to methods of selecting a therapy for an autoimmune disease wherein the method comprises a step (a) of identifying a TCR V gene expressed by a target cells and step (b) comprises selecting a therapy that targets T cells. The claims do not clarify how one selects a therapy. It is unclear as to whether the method steps are intended to be completely unrelated such that regardless of the outcome of step (a) any type of therapy is selected or if the outcome of step (a) determines the selection of therapy in step (b).

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 8-10, 12-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Chou (Journal of Neuroscience Research (1996) 45: 838-851).

Chou teaches a method which comprises the steps of: (a) determining the expression of one or more TCR Vβ genes by T cell clones isolated from individuals with multiple sclerosis; and (b) determining regulatory activity elicited in response to one or more of the TCR V peptides by T cells from said individual (page 841). In particular, step (a) is performed by RT-PCR amplification of TCR Vβ gene sequences and step (b) is performed by analyzing the secretion of anti-inflammatory antigens including IL-10 and IL-4. Chou (page 841-842) teaches that two CDR2 peptides, Vβ5.2-38-58 and Vβ6.1-38-58 are over-expressed by MBP-specific T cell clones from progressive MS patients. Chou analyzed T cell regulatory activity elicited in response to TCR V peptides following immunization. The reference teaches that 6 of 8 patients immunized with either Vβ5.2 or Vβ5.2 plus Vβ6.1 peptides had increased peptide specific T cell frequencies. Chou concludes that the TCR V-reactive T cells differ in their cytokine message profiles and soluble inhibitory activity. It is noted that the recitation of "is identified as a V gene expressed by target T cells" is considered to be a mental step. Similarly, the recitation in claims 23-25 of "selecting a therapy" is also a mental step. The method steps recited in the present claims are identical to those taught by Chou and the recitation of "identifying a T cell receptor (TCR) variable (V) gene expressed by target T cells" does not distinguish the claimed invention over that of Chou because the method of Chou necessarily results in the identification process. These recitations do not result in manipulative differences in the method steps when compared to the prior art.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chou in view of Goodwin (U.S. Patent No. 5,569,585)..

Chou teaches a method which comprises the steps of: (a) determining the expression of one or more TCR Vβ genes by T cell clones isolated from individuals with multiple sclerosis; and (b) determining regulatory activity elicited in response to one or more of the TCR V peptides by T cells from said individual (page 841). In particular, step (a) is performed by RT-PCR amplification of TCR Vβ gene sequences and step (b) is performed by analyzing the secretion of anti-inflammatory antigens including IL-10 and IL-4. Chou (page 841-842) teaches that two CDR2 peptides, Vβ5.2-38-58 and Vβ6.1-38-58 are over-expressed by MBP-specific T cell clones from progressive MS patients. Chou analyzed T cell regulatory activity elicited in response to TCR V peptides following immunization. The reference teaches that 6 of 8 patients immunized with either Vβ5.2 or Vβ5.2 plus Vβ6.1 peptides had increased peptide specific T cell frequencies. Chou concludes that the TCR V-reactive T cells differ in their cytokine message profiles and soluble inhibitory activity. It is noted that the recitation of "is identified as a V gene expressed by target T cells" is considered to be a mental step. Similarly, the recitation in claims 23-25 of

"selecting a therapy" is also a mental step. The method steps recited in the present claims are identical to those taught by Chou and the recitation of "identifying a T cell receptor (TCR) variable (V) gene expressed by target T cells" does not distinguish the claimed invention over that of Chou because the method of Chou necessarily results in this identification process. These recitations do not result in manipulative differences in the method steps when compared to the prior art. Chou teaches T cell clones that are characterized as exhibiting a CD4+ and $CD45RA^{lo}$ memory cell phenotype. Chou does not characterize the cells as being CD25+ and CD45RO+.

Goodwin teaches characterizing T cells for their surface markers and specifically teaches analyzing cells for the markers CD45RO, CD45RA and CD25. The reference teaches that CD45RO+ cells are generally regarded as activated memory cells and that CD45RA+ cells are generally regarded as naive cells (columns 17-18). The reference also teaches that CD25 is a marker for activated T cells (column 21).

In view of the teachings of Goodwin, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Chou so as to have analyzed T cells that are CD25+ and CD45RO+ in order to have provided a method which specifically analyzed cells types that constitute activated T cells.

6. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chou in view of Czerkinsky (cited in the IDS of October 5, 2001).

Chou teaches a method which comprises the steps of: (a) determining the expression of one or more TCR Vβ genes by T cell clones isolated from individuals with multiple sclerosis; and

(b) determining regulatory activity elicited in response to one or more of the TCR V peptides by T cells from said individual (page 841). In particular, step (a) is performed by RT-PCR amplification of TCR Vβ gene sequences and step (b) is performed by analyzing the secretion of anti-inflammatory antigens including IL-10 and IL-4. Chou (page 841-842) teaches that two CDR2 peptides, Vβ5.2-38-58 and Vβ6.1-38-58 are over-expressed by MBP-specific T cell clones from progressive MS patients. Chou analyzed T cell regulatory activity elicited in response to TCR V peptides following immunization. The reference teaches that 6 of 8 patients immunized with either Vβ5.2 or Vβ5.2 plus Vβ6.1 peptides had increased peptide specific T cell frequencies. Chou concludes that the TCR V-reactive T cells differ in their cytokine message profiles and soluble inhibitory activity. It is noted that the recitation of "is identified as a V gene expressed by target T cells" is considered to be a mental step. Similarly, the recitation in claims 23-25 of "selecting a therapy" is also a mental step. The method steps recited in the present claims are identical to those taught by Chou and the recitation of "identifying a T cell receptor (TCR) variable (V) gene expressed by target T cells" does not distinguish the claimed invention over that of Chou because the method of Chou necessarily results in this identification process. These recitations do not result in manipulative differences in the method steps when compared to the prior art. Chou teaches analyzing cytokine expression by PCR. Chou does not teach analyzing cytokine expression by an immunospot assay.

Czerkinsky teaches methods of analyzing cytokine expression by an ELISPOT assay. The reference teaches that this method is advantages because it provides an effective means for analyzing cytokine expression by single cells (page 34-35).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Chou so as to have analyzed cytokine expression using the ELISPOT assay in order to have achieved the benefits of providing an equally effective method for analyzing cytokine expression and for performing such methods using single cells.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Chou (reference cited in the IDS of October 5, 2001; Journal of Immunology. 1994. 152: 2520-2529) teaches the TCR V profiles of the T cell clones analyzed by Chou (1996). Chou teaches that 11 of the 19 T cell isolates expressed only a single Vβ clone (page 2523).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306 or (703)-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

CARLA J. MYERS
PRIMARY EXAMINER

February 20, 2003